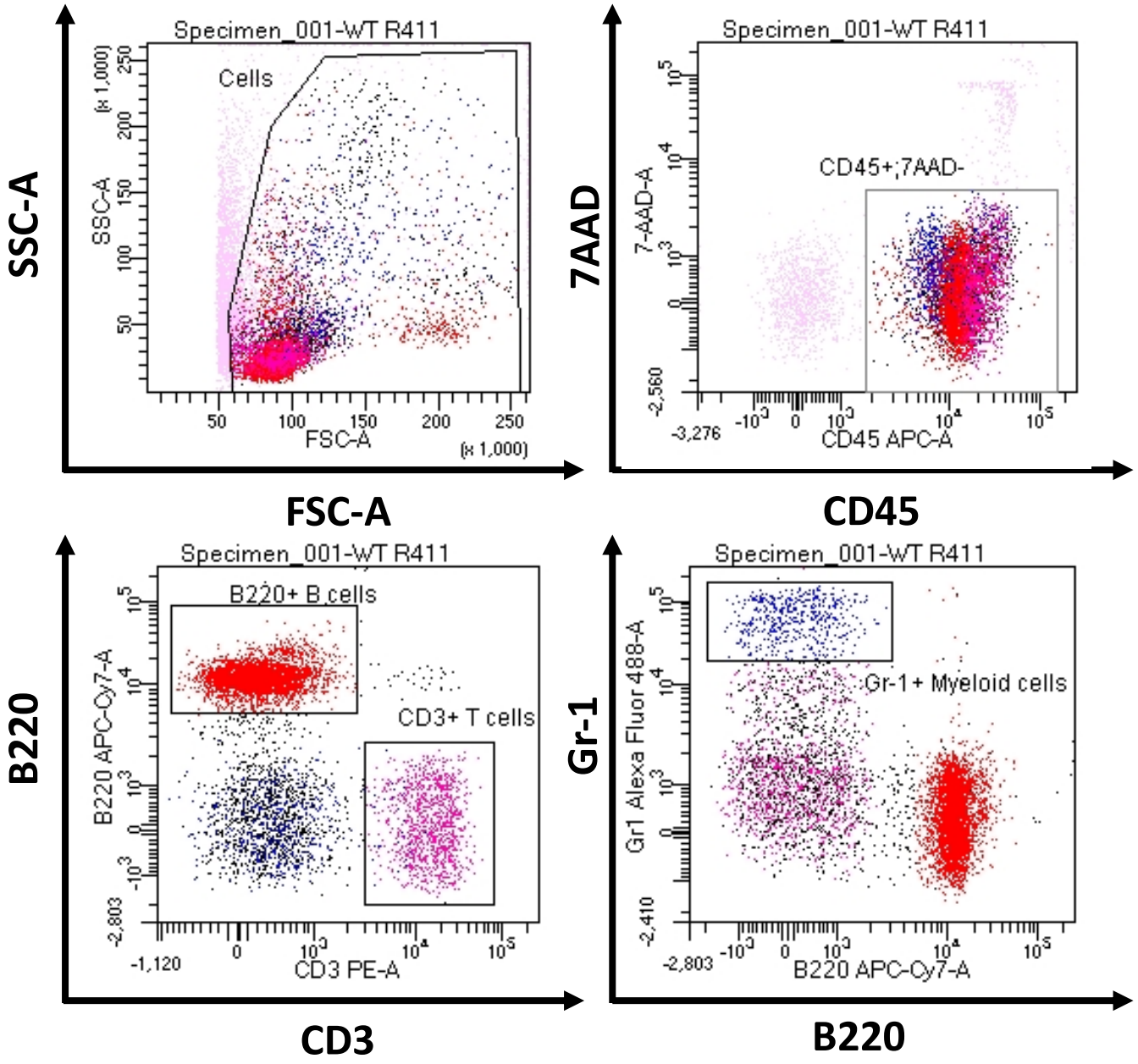
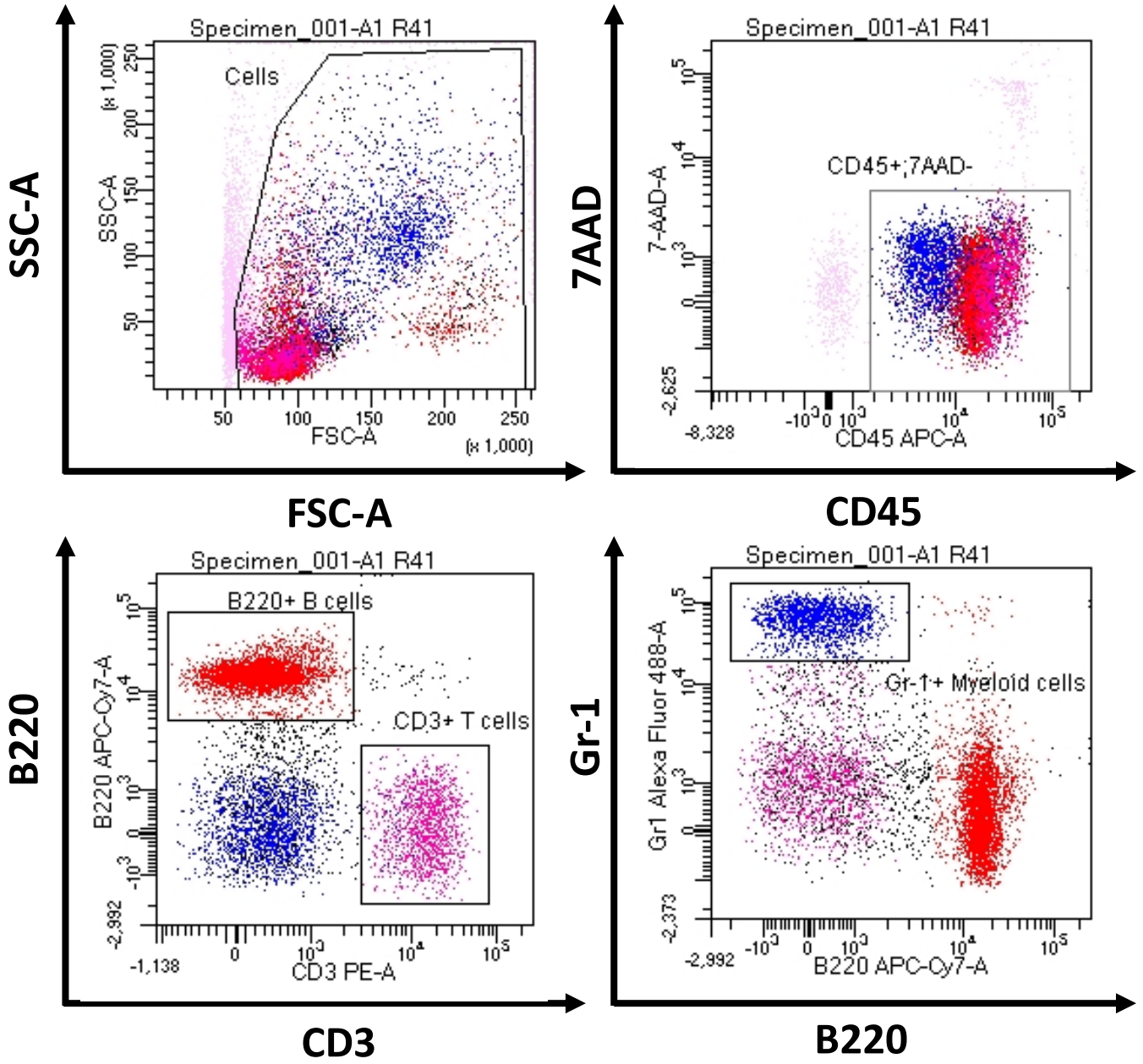
Supporting Information for

The retinoic acid hydroxylase Cyp26a1 has minor effects on postnatal vitamin A homeostasis, but is required for exogenous *at*RA clearance

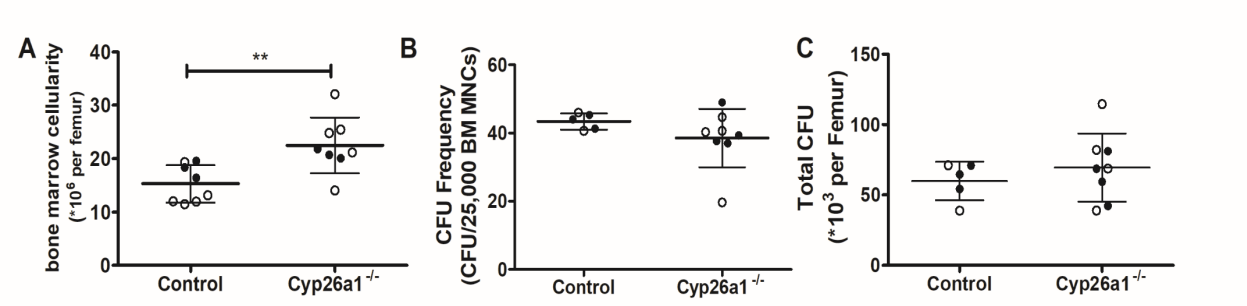
Guo Zhong[1], Cathryn Hogarth[2], Jessica Snyder[3], Laura Palau[4], Traci Topping[2], Weize Huang[1], Lindsay Czuba[1], Jeffrey LaFrance[1], Gabriel Ghiaur[4], Nina Isoherranen[1,*]



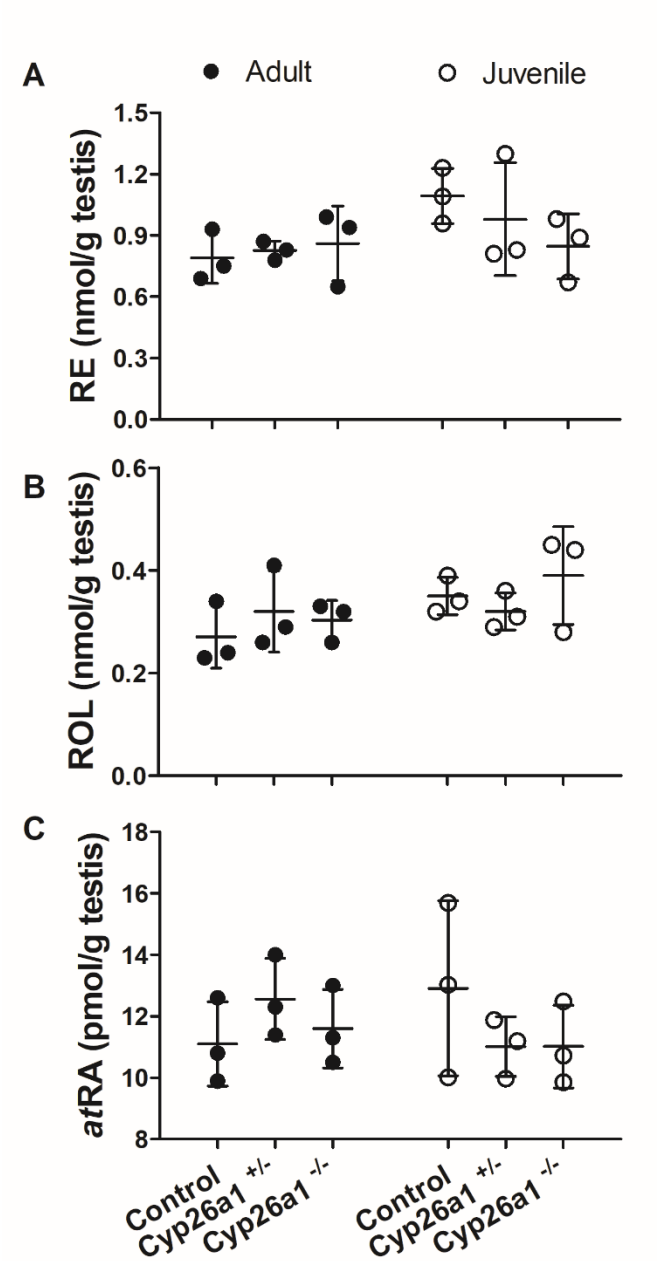
Supplemental Figure S1. Representative peripheral blood Flow Cytometry plots for *Cyp26a1*$^{+/+}$ mice. Cells are selected and gated to be 7AAD negative or alive and CD45+. B220+ cells are classified as B cells, CD3+ cells as T cells and Gr-1+ as myeloid cells.



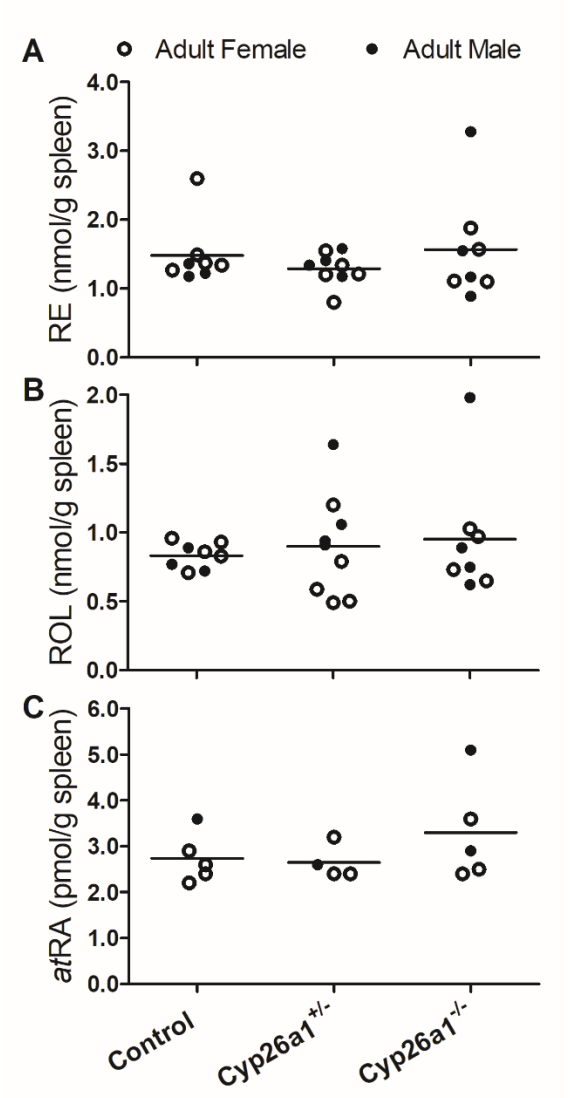
Supplemental Figure S2. Representative peripheral blood Flow Cytometry plots for *Cyp26a1*$^{-/-}$ mice. Cells are selected and gated to be 7AAD negative or alive and CD45+. B220+ cells are classified as B cells, CD3+ cells as T cells and Gr-1+ as myeloid cells.



Supplemental Figure S3. Analysis of A) bone marrow (BM) cellularity, B) CFU frequency in BM and C) absolute number of CFU in BM obtained from *Cyp26a1*$^{+/+}$ (control) and *Cyp26a1*$^{-/-}$ mice. Horizontal lines indicate mean values and error bars indicate S.D.. Each data point represents an individual mouse. The filled and open symbols represent male and female mice, respectively.



Supplemental Figure S4. Testis retinoid concentrations in *Cyp26a1*$^{-/-}$ mice in comparison to *Cyp26a1*$^{+/-}$ and *Cyp26a1*$^{+/+}$ (control) mice. The knock-out of *Cyp26a1* was induced either in adult (closed symbols) or juvenile (open symbols) animals as described in the methods section. In all panels, the horizontal lines indicate mean values and error bars indicate S.D.. Each data point represents an individual mouse. There were no differences in testis concentrations of any of the retinoids between genotypes.



Supplemental Figure S5. Analysis of concentrations of A) retinyl esters (RE), B) retinol (ROL) and C) *at*RA in spleen samples from *Cyp26a1*$^{+/+}$ (control), *Cyp261*$^{+/-}$ and *Cyp26a1*$^{-/-}$ adult mice. The horizontal lines indicate mean values and each data point represents an individual mouse.

Supplemental Table S1. Input values of all pharmacokinetic, physicochemical, and physiological parameters used in the semi-physiologically-based model to simulate *at*RA disposition. Physiological parameters including volumes and blood flows are extracted from real mice data based on Brown RP, Delp MD, Lindstedt SL, Rhomberg LR, Beliles RP. Physiological parameter values for physiologically based pharmacokinetic models. Toxicol Ind Health. 1997;13(4):407-84.

Parameter	Unit	Value
$k_{f,fast}$	nmol/hr	0
$k_{f,slow}$	nmol/hr	15
$k_{f,liver}$	nmol/hr	2
$V_{central}$	L	0.001
V_{fast}	L	0.003
V_{slow}	L	0.015
V_{liver}	L	0.001
$Q_{cardiac\ output}$	L/hr	6
Q_{fast}	L/hr	2.5
Q_{slow}	L/hr	2.5
Q_{liver}	L/hr	1
$f_{u,p}$	-	1
B/P	-	1
$K_{p,fast}$	-	1
$K_{p,slow}$	-	1
$K_{p,liver}$	-	3.79
$CL_{int,fast}$	L/hr	0
$CL_{int,slow}$	L/hr	10
$CL_{int,liver}$	L/hr	0.03
CL_{pd}	L/hr	10,000
$K_{m,cyp26a1}$	nmol/L	1,000
$K_{m,cyp26b1}$	nmol/L	10
k_a	hr^{-1}	1
i.p. dose	nmol	500